Diese Website verwendet Cookies von Google, um Dienste anzubieten und den Traffic zu analysieren. Deine IP-Adresse und dein User-Agent werden zusammen mit Messwerten zur Leistung und Sicherheit für Google freigegeben. So können Nutzungsstatistiken generiert, Missbrauchsfälle erkannt und behoben und die Qualität des Dienstes gewährleistet werden.

WEITERE INFORMATIONEN OK

Monday, September 22, 2008

Patent goo: self-replicating Paxil

In his novel Cat's Cradle, science fiction writer Kurt Vonnegut postulated "Ice-9." Ice-9 was a form of water that was frozen at room temperature and catalyzed any normal water it came in contact with into more crystals of Ice-9. Once released into the environment, it froze all water, including us. Eric Drexler in the 1980s raised the specter of nano-robots that made copies of themselves and ate everything in their path: "gray goo." A wide variety of similar hypothetical disasters have since been given referred to as some sort of "goo."

Self-replicating chemicals are not merely hypothetical: since Cat's Cradle, scientists have discovered some real-world example of crystals that seed the environment, converting other forms (polymorphs) of the crystal into their own. The population of the original polymorph diminishes as it is converted into the new form: it is a "disappearing polymorph." In 1996 Abbott Labs began manufacturing the new anti-AIDS drug ritonavir. In 1998 a more stable polymorph appeared in the American manufacturing plant. It converted the old form of the drug into a new polymorph, Form 2, that did not fight AIDS nearly as well. Abbott's plant was contaminated, and it could no longer manufacture effective rintonavir. Abbott continued to successfully manufacture the drug in its Italian plant. Then American scientists visited, and that plant too was contaminated was contaminated and could henceforth only produce the ineffective Form 2. Apparently the scientists had carried some Form 2 crystals into the plant on their clothing.

Another instance of the "disappearing polymorph" may be the anti-depressant, Paxil (U.S. brand name for the chemical paroxetine hydrochloride). No, self-replicating Paxil doesn't naturally spread into our brains and make people happy for free. It's not "happy goo." On the contrary, self-replicating Paxil converted, according to one of the parties in the ensuing lawsuit, an old, and now off-patent, form of Paxil into a new, patented form of Paxil. Once the new form, the hemihydrate form of Paxil, was created, its crystals started floating about, converting small fractions of the old form, anhydrous Paxil, into hemihydrate. Both forms of the drug work equally well as an anti-depressant, but it became impossible to manufacture the off-patent anhydrate without some of it being converted into the patented form. Call it "patent goo."

Apotex, a generic drug manufacturer, was all set up to manufacture the off-patent anhydrous generic Paxil when it discovered small fractions of it were being converted into the hemihydrate. They couldn't remove the contamination. Smithkline, owner of the patent on the hemihydrate, sued them for patent infringement. Apotex argued that the hemihydrate form occurred naturally, so that Smithkline's patent was invalid. Smithkline argued that it was a disappearing polymorph, that the hemihydrate form had not existed before they had created it in their labs, and that it was up to Apotex to remove the hemihydrate from its product or pay it a royalty. Apotex was unable to remove the hemihydrate and unwilling to pay a royalty.

About Me

Nick Szabo

"A premier thinker about history, law and economics, and the lessons they have for security." -- Adam Shostack, Emergent Chaos

"Szabo comes out with these essays that leave me in awe." -- Brian Dunbar

"Reading material that is eclectic, challenging and endlessly fascinating." -- Sean McGrath, Propylon

"Like most blogs worth my attention, this blog is updated only infrequently. That is because the authors of blogs worth my attention only post when they have something to say that is true, relevant and not already known by their audience. Most of the human race does not have the skill to know when an idea has these three properties. The skill is particularly rare in the fields of politics and economics, which is why this blog is such a rare and valuable thing." -- Richard Hollerith

View my complete profile

Judge Richard Posner heard this case in the trial court and wrote an opinion that contains a good explanation of the self-replicating Paxil controversy. The Federal Circuit heard the appeal and decided that Smithkline's patent on the hemihydrate was invalid as "inherently anticipated" because anhydrate naturally converts into hemihydrate. Normally, anticipation would require an actual reference describing the claimed chemical structure (in patent lingo that the hemihydrate was "taught in the prior art"). But Judge Rader held that inherent anticipation occurs when, more likely than not, an operation that is taught in the prior art would result in the claimed chemical. The anhydrate which was taught in the prior art would more than likely result in natural creation of some hemihydrate. Judge Gajarsa in concurrence argued that the drug was discovered not invented, making it unpatentable subject matter. Gajarsa's opinion may have inspired the United States Supreme Court to raise the subject matter issue on its own (i.e., it had not been argued by the parties to the case) in *Metabolite*. The Supreme Court is considering whether to take the appeal on the self-replicating Paxil case as well.

Posted by Nick Szabo at 5:41 PM

7 comments:

brett jordan said...

Great article Nick, thanks. BTW, looks like you've got a self-replicating version of the phrase 'was contaminated' :-) oh, the irony!!!

10:46 AM

Anonymous said...

this is awfully similar to the prion disease debate (i'm no expert). It's interesting, especially reading biologists that cannot fathom an infection without a living agent (virus, bacterium, parasite etc...)

6:00 AM

Nick Szabo said...

This comment has been removed by a blog administrator.

11:41 AM

Nick Szabo said...

Thanks, Brett. Anonymous, that's a very interesting point about prions, enough to inspire me to blog on the subject.

DNA, RNA, prions, and disappearing polymorphs are all "replicators" as Richard Dawkins puts it. Only the first three replicate in animals.

Nick Szabo
http://unenumerated.blogspot.com
http://szabo.best.vwh.net

11:48 AM

Blog Archive

- ► 2018 (1)
- ► 2017 (3)
- ► 2016 (4)
- ► 2015 (3)
- ► 2014 (3)
- ► 2013 (3)
- ► 2012 (8)
- ► 2011 (12)
- ► 2010 (9)
- ► 2009 (29)
- ▼ 2008 (55)
  - ► December (2)
  - ► October (2)
  - ▼ September (4)
    - Patent goo: self-replicating Paxil
    - The kula ring
    - A letter from the industrial revolution
    - The principle of least authority
  - ► August (9)
  - ► July (4)
  - ► June (6)
  - ► May (6)
  - ► April (4)
  - ► March (10)
  - ► February (5)
  - ► January (3)
- ► 2007 (47)
- ► 2006 (130)
- ► 2005 (44)

Joel said...

This is good news for accidental GMO farmers, who have "infringed" by allowing patented pollen to float in on the breeze.

9:41 AM

Anonymous said...

Apparently, safety signs were ignored: http://cache.io9.com/assets/images/io9/2008/08/Smoky_The_Nanobot.jpg

4:39 PM

Bryce Evaristo said...

Why would a biologist not fathom a non living infection when it's common knowledge that non living infections in both animals and humans are quite prevalent and one of the most notorious would be HIV or the prions you first mentioned (although I have to admit I'm so fascinated by how HIV works and replicates and I believe the cure to HIV lies in the virus because it has virtually no proofreading when it replicates which can slightly alter the virus if the right "error" happens when the virus replicates itself it's possible that the new version/mutation will not be able to attach itself to receptor sites and in theory it would be possible for an individual to be "spontaneously" cured due to the virus making an error and ultimately not being able to continue in its new form inside its host

So I wonder if the future of an HIV cure is not some advanced antiviral drug but rather a "controlled" mutation of the virus itself and then introduce that modified HIV into the people already infected with the regular types or some variation of the sort

Prions on the other hand I recently read about a year ago and find them to be way more sinister and horrid in both how they spread and where

disregard my reply to your original post considering it's been almost a decade and whatnot

3:52 PM

Post a Comment

Newer Post Home Older Post

Subscribe to: Post Comments (Atom)

Simple theme. Powered by Blogger.